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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,915	09/24/2003	Richard Daifuku	021227-000310US	6525

20350 7590 05/02/2007

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

MAIL DATE	DELIVERY MODE
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,915	DAIFUKU ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's amendments and remarks filed on 02/15/2007 are acknowledged. Claims 2-7 and 16-28 have been canceled. Claim 1 has been amended.

The rejections under 35 U.S.C. 112, first paragraph; 35 U.S.C. 112, first paragraph; and 35 U.S.C. 102(b) of the Office Action dated 11/16/2006 have been overcome by the applicant's amendments.

Claims 1 and 8-15 are currently pending in this application.

The following is new rejection(s) necessitated by Applicant's amendment filed on 02/15/2007.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-15 and the amended claim 1 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Driscoll et al. (Driscoll) (U.S. Patent No. 4,788,181) in combinations with Wierenga (U.S. Patent 4,140,850) in view of Meyer et al. (Meyer) (U.S. Patent 5,574,142) of record.

Like the instantly claimed invention, the Driscoll's patent teaches the cytidine and dideoxycytidine compounds and their monophosphates wherein $R^1 = NH_2$; Y = N or C; R^7= alkyl or H; R^3= '=O'; R^8= H; Z=C; R^2= H; R^{4a}= H or OH; R^4= H or OH; R^5= H or OH and R^6= CH_2OH (see structures in col.2, lines 60-65; col. 3-4, Scheme I, 4 & 10; col. 5,

16 & 18-21; col.6, 1 & 24; and col.7, 3 &26). The prior art discloses that said compounds are useful in the anti-viral therapy, both against RNA viruses and against DNA viruses (col.2, lines 37-39). In the amended claim 1, there is one point of unsaturation at the 3,4-position and the 5-position being substituted with R^8, an unsubstituted alkyl, however Driscoll discloses compounds of structure 4 and 7 (col.3 to 4) wherein there are two unsaturations at the position 3,4 and 5,6, it would have been obvious to one skilled in the art to accomplish a compound with only one point of unsaturation at the 3,4-position and the 5-position being substituted with R^8, an unsubstituted alkyl, through routine experimentation in the absence of unexpected results with a particular combination. Furthermore, Driscoll's patent discloses that any substitution on nucleoside compound such as in the structure 1 in col.6 can make the compound more susceptible to penetration of the blood-brain barrier and therefore effective against the AIDS virus in brain (col.7, lines 58-63). The Driscoll's patent also discloses that said nucleoside compounds can be phosphorylated at the C-5' position to form nucleotides; both the unphosphorylated and the phosphorylated compounds can be administered to an infected host via orally, intravenously, or the like (col.3, lines 57-60). The prior art discloses that the lower doses of monophosphorylated nucleoside compounds can be required for the protection of HTLV-III/LAV infected cells because their triphosphate formation is facilitated when penetrated the cell membrane (col.7, lines 25-36). Therefore, with regard to claims 8 and 10 wherein C-5' is phosphorylated with the group R^6, it would be within the scope of the artisan in this art to accomplish the nucleotides of said compounds through routine experimentation by phosphorylating the

C-5' position to form nucleotides because the prior art teaches that the triphosphate formation of a monophosphorylated nucleoside is facilitated when a monophosphorylated nucleoside is penetrated into the cell membrane conjugates, in the absence of unexpected results with a particular combination.

It is noted that in the compound claims 9 and 11, the recitation of an intended use such *in vivo* cleavage of said compound after entry into a cell not afforded any patentable weight.

The Wierenga's patent teaches the nucleoside compounds wherein R^1 = '=O'; Y = N; R^7= alkyl; R^3= '=O'; R^8= H; Z=C; R^2= '=O'; R^{4a}= OH; R^5= OH and R^6= CH_2OH (see structures in col.2, lines 20-30; col.5 to col. 8, Table I & II). Silicon substituted hydroxyl group of a ribose moiety is also disclosed (col.10, lines 45-55). The pharmaceutical preparations of said compounds are useful for their activity *in vitro* against various susceptible DNA viruses (col.5, lines 1-20).

The formulation of claims 12-15 differs from the Driscoll and Wierenga's patents by claiming a formulation of nucleoside compound and a second compound A-B of claim 12. The Driscoll and Wierenga's patents teach a pharmaceutical composition of said nucleosides in the absence of a second compound A-B and a polycationic carrier. It is noted that the Driscoll patent does not teach a phosphorus moiety substituted with a linker "L".

Meyer teaches the pharmaceutical compositions containing oligonucleotides covalently linked through a peptide moiety to a carrier moiety, which facilitates delivery of said drug (col. 1, lines 5-10). Meyer discloses surfactant carriers similar to instantly claimed A-B, having a hydrophilic and a hydrophobic residue (col.4, lines 27-35 and Fig. 7). Meyer discloses a nucleotide (ODN) with a modified phosphor-di-ester group wherein the C-5' position of the nucleoside is linked to a phosphate group having an alkyl group linker (Fig.3). Meyer also discloses the use of polyamine carriers or cationic macromolecules in the composition to enhance the cellular uptake of said composition (col.4, lines 37-49). The polycationic carriers such as dendrimers are disclosed (Fig.9). Meyer discloses said composition in aqueous form for topical application (col. 19, lines 26-27).

It would have been obvious to person having ordinary skill in the art at the time the invention was made having the above-cited references before him, to select any substitution for variable $R^1 - R^{18}$ in nucleoside compounds as taught by the Driscoll and Wierenga's patents and combining with a second compound A-B and a polycationic carrier to form a formulation to enhance the cellular uptake of said composition as taught by Meyer. The motivation is provided by the Driscoll patent because Driscoll disclosed that the lower doses of said monophosphorylated nucleoside compounds are needed for the protection of HTLV-III/LAV infected cells because their triphosphate formation is facilitated when said compounds are penetrated into the cell membrane (col.7, lines 25-36).

Rejection Maintained

Rejection of claims 1 and 8-15 under 35 U.S.C. 103(a) is maintained for the reasons of record.

Applicant's arguments traversing the rejection of claims 1 and 8-15 under 35 U.S.C. 103(a) have been fully considered but they are not persuasive.

Response to Arguments

Applicant argue, "The 1,3,5-triazine of Driscoll cannot be substituted at the 5-position without making a quaternary nitrogen, and does not teach an unsubstituted alkyl in the 5-position of the triazine ring. Thus, the compounds of Driscoll fail to teach all the lements of the amended claims."

In the amended claim 1, there is one point of unsaturation at the 3,4-position and the 5-position being substituted with R^8, an unsubstituted alkyl, however Driscoll discloses compounds of structure 4 and 7 (col.3 to 4) wherein there are two unsaturations at the position 3,4 and 5,6, it would have been obvious to one skilled in the art to accomplish a compound with only one point of unsaturation at the 3,4-position and the 5-position being substituted with R^8, an unsubstituted alkyl, through routine experimentation in the absence of unexpected results with a particular combination.

2. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07 (a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
April 30, 2007